Dissertation on

" EVALUATION OF EFFICACY OF PROPHYLACTIC ORAL EPHEDRINE IN PREVENTION OF HYPOTENSION FOLLOWING SUBARACHNOID BLOCK IN ELECTIVE LOWER ABDOMINAL AND SCROTAL SURGERIES "

Submitted to the

TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
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ANAESTHESIOLOGY

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CERTIFICATE

This is to certify that the dissertation " **EVALUATION OF EFFICACY OF PROPHYLACTIC ORAL EPHEDRINE IN PREVENTION OF HYPOTENSION FOLLOWING SUBARACHNOID BLOCK IN ELECTIVE LOWER ABDOMINAL AND SCROTAL SURGERIES** " presented herein by **Dr.G.ILANGO,** is an original work done in the Department of Anesthesiology, Government Stanley Medical College and Hospital, Chennai, in partial fulfillment of regulations of the Tamilnadu Dr.M.G.R.Medical University for the award of degree of M.D. (Anesthesiology) Branch X, under my guidance and supervision during the academic period 2004-2007.

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DECLARATION

I **Dr.G.ILANGO** solemnly declare that this dissertation, titled "**EVALUATION OF EFFICACY OF PROPHYLACTIC ORAL EPHEDRINE IN PREVENTION OF HYPOTENSION FOLLOWING SUBARACHNOID BLOCK IN ELECTIVE LOWER ABDOMINAL AND SCROTAL SURGERIES "** is a bonafied record of work done by me in the Department of Anesthesiology, Stanley Medical College and Hospital, Chennai, under the guidance of **Prof. R. Meenakshi, M.D., D.A.,** Professor and H.O.D., Department of Anesthesiology, Government Stanley Medical College & Hospital, Chennai - 600 001.

This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of M.D. (Anesthesiology), Branch X, examination to be held in February 2007.

Place: Chennai

Date: **Dr. G.ILANGO**

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CONTENTS

INTRODUCTION

Spinal anaesthesia or subarachnoid block as it is popularly called is one of the regional anaesthetic techniques achieved by blocking the spinal nerves in the subarachnoid space, by injecting local anaesthetic agent into the sub arachnoid space.[1]

Sub arachnoid block is commonly used in surgeries of the Lower abdomen and lower limbs.

Though it is a blind procedure, it is easy to perform and gives good intensity of sensory, motor & sympathetic blockade of rapid onset. Depending upon the local anaesthetic injected the duration of blockade varies.

Spinal anaesthesia[2] has the advantage over General anaesthesia in preventing the sympathetic response from laryngoscopy and intubation. However it is not devoid of fatal complications of which hypotension and bradycadia are the hemodynamic complications resuting in significant morbidity and mortality.

Many factors have been found to result in hypotension in midthoracic level subarachnoid block[1] of which important ones are

(1) sympathetic blockade leading to decrease in systemic vascular resistance thereby causing hypotension.

(2) Increased venous capacitance reducing the venous return causing decreased cardiac output leading to hypotension.

(3) Bradycardia again by reducing the cardiac output results in hypotension.

Hence it is of paramount importance to treat hypotension and its complications but prevention is better than allowing it to happen and treating it .Various methods have been tried to prevent hypotension.[1]

1. parenteral administration of vasopressors

2. preloading with crystalloids and colloids and

3.using compression stocking or pneumatic devices in the lower limbs to improve venous return.

Parenteral administration of ephedrine[3] for prevention of hypotension has been tried in various clinical studies but not much studies have been done to know the efficacy of prophylactic oral administration of ephedrine.

Therefore a prospective randomized clinical study is done to determine the efficacy of prophylactic oral ephedrine in reducing the incidence of hypotension following subarachnoid block in patients undergoing elective lower abdominal and scrotal surgeries.

AIM OF THE STUDY

Aim of this study is to determine the efficacy of prophylactic oral ephedrine administered before subarachnoid block in minimising the incidence of spinal anaesthesia induced hypotension in patients undergoing elective lower abdominal and scrotal surgeries.

HISTORY OF SPINAL ANAESTHESIA[1]

Cerebrospinal fluid was discovered by Domenico Cotugno in 1764. Its circulation was described by F. Magendie in 1825.

The first spinal analgesia was introduced to this world in 1885 by Leonard corning, a New York neurologist when he accidentally pierced the dura while experimenting cocaine on spinal nerves of a dog. Later in 1891 Heinrich Irenaeus Quincke standardized lumbar puncture as a simple clinical procedure.

The first planned spinal analgesia for surgery in man was performed by august Bier on 16th August 1898. He injected 3ml of 0.5% cocaine solution into a 34 year old man.. In 1903 adrenaline was used to increase the duration and reduce the toxicity of spinal analgesia.

Ephedrine was introduced in 1923 by Chen and Schmidt. It was used for maintaining blood pressure in spinal analgesia in 1927 by Ocherblad, Dillon, Rudolf and Graham. In Earlier years the special attention was with the advancement of spinal anaesthesia. The reasons being:

(i) The end point of CSF return was well defined.

(ii) Spinal anaesthesia produced superb skeletal muscle relaxation facilitating surgical exposure at the time when muscle relaxants had not been introduced.

These advantages of spinal anaesthesia historically created many enthusiastic clinicians. Newer drugs like stovaine, procaine, spinocaine, duracaine were being discovered. Spinal anaesthesia was being used for surgeries in abdomen, head, neck and thorax.

Morton promoted high spinal anaesthesia for surgical procedures carried out on the head and neck.

Koster used total spinal blockade for thoracic and intracranial procedures. Spinal anaesthesia was not limited to surgical conditions but was used for treatment of medical conditions (eg. Pulmonary edema) by taking advantage of its venodilatory effect.

Anaesthesiologists continue to face confusion about balancing the risks and benefits of spinal anaesthesia.

One impediment to the effective use of neuraxial block is the predictable decrease in arterial blood pressure and heart rate through the accompanying sympathetic blockade with its attendant vasodilatation and blockade of cardioaccelerator fibres.

ANATOMY RELATED TO THE SUBARACHOID BLOCK[4]

The vertebral column consists of 7 cervical, 12 thoracic, 5 lumbar, 5 sacral and 4 to 5 coccygeal vertebrae.

The Vertebral column has two primary curves, thoracic and sacral which are concave anteriorly, two secondary curves namely cervical and lumbar. The intervertebral disc makes up for one-quarter of the length of vertebral column.

The Vertebral canal is bounded in front by bodies of the vertebrae and intervetebral disc, posteriorly by the laminae, ligamenta flava and the arch.

Contents of the vertebral canal are ,

(i) roots of spinal nerves,

(ii) spinal membranes with their enclosed cord and cerebrospinal fluid

(iii)structure like vessels, fat and areolar tissue of epidural space.

The vertebral ligaments binding the canal are:

(i) Supraspinous ligament.

(ii) Interspinous ligament

(iii) Ligamenta flava

(iv) Posterior longitudinal ligament

(v) Anterior longitudinal ligament

Spinal cord is the elongated part of the Central Nervous system which occupies upper two – thirds of the vertebral canal and is approximately 45 cms long in adults.

It extends from upper border of atlas to upper border of 2nd lumbar vertebra. Below it ends in conus medullaris, from the apex of which filum terminale descends as far as coccyx. In adults the spinal nerve roots pass out obliquely through the intervertebral foramen. The lumbar and sacral nerve roots, descend almost vertically to meet their foramina and are known as cauda equinae.

The spinal cord is ensheathed by three membranes from outwards to inwards.

Duramater : The spinal duramater represents only the inner or meningeal part, outer part is represented by the periosteum lining the vertebral canal. A strong fibrous layer forms a tubular sheath attached above to the margins of foramen magnum and ending below at lower border of S2 sacral vetebra.

Arachnoid : This is a thin transparent sheath closely applied to

the dura, surrounding the cranial and spinal nerves as far as their point of exit from skull and vertebral canal.

Pia Mater: This is separated from the arachnoid by the subarachnoid space filed with cerebrospinal fluid. The piameter closely invests the cord and sends septa into its substance. A lateral fibrous band called denticulate ligament projects into the subarachnoid space. A posterior midline septum, has been described. It ends as the filum terminale which pierces the distal end of dural sac and is attached to the periosteum of coccyx .

Subdural space is a potential space between dura and the arachnoid. Injection of local analgesic into it may cause inadequate or abnormally high block,.

Subarachnoid space lies between arachnoid and piamater. The contents of the space are the spinal nerve roots, the denticulate ligaments, a spongy reticulum of fibres connecting the pia to the arachnoid, cerebrospinal fluid, the larger vessels and spinal nerves.

Anterior root is efferent and motor. Sympathetic preganglionic axons arise from cells in the intermedio lateral horn of the spinal cord from T1 to L2.Posterior root is larger and has a ganglion and conveys fibres of (i) Pain, (ii) Tactile (iii) Thermal (iv)Deep pressure and proprioception (v)

afferents from the viscera and (vi) Vasodilator fibres.

The anterior and posterior roots with its covering of pia , arachnoid and dura crosses extradural space and unite in the intervertebral foramen to form the main spinal nerve trunks which soon divide into anterior and posterior primary divisions.

BLOOD SUPPLY TO THE SPINAL CORD

- Poster spinal arteries, two on each side, branch from posterior inferior cerebellar arteries; it supplies the posterior column of spinal cord.
- Anterior spinal Artery, a single vessel, branch from the junction of two small branches from each vertebral artery. It supplies lateral and anterior columns, about 3/4th of the substance of the spinal cord. It receives communications from the intercostal, lumbar and other small arteries. Communicating branches at the level of T10 and T11 larger than the others and help to supply the enlargements of cord.

Extra dural veins :They largely form a plexus, most dense in the anterolateral part of the extradural space. They receive blood from the cord and the vertebral canal with its contents and communicate with both the intracranial sinuses and the tributaries of the inferior vena cava and the azygos system.

NERVE SUPPLY OF MENINGS

The posterior aspect of the dura and arachnoid contains no nerve fibres and so no pain is felt on dural puncture. The anterior aspect is supplied by spinovertebral nerves.

PHYSIOLOGY RELATED TO SUBRACHNOID BLOCK[4]

Zone of Differential Block:

Sensory : In intradural block sympathetic fibres are blocked 2 to 6 segments higher than sensory fibres. Sympathetic blockade will be greater when more concentrated solutions are used (or) when adrenaline is used.

Motor: In intra dural blockade, the difference between sensory and motor block is slight (two segments). Motor block is two segments below sensory block.

Differential action of local anaesthetic on nerve fibre :

All types of nerve fibres are affected by local anaesthetic agent, there is a tendency for small, slow conducting fibres to be more rapidly blocked than large fast conducting fibres.

In case of medium sized fibres however, these rules do not hold good. Myelinated preganglionic beta fibres which have faster conduction time are about three times more sensitive to blockade than slower post ganglionic C-fibres.

The Order of Sensitivity to Blockade seems to be (Collins et al)

a. Preganglionic sympathetic fibres – Vasomotor blockade – dilatation of cutaneous blood vessels – increases cutaneous blood flow.

b. Temperature fibres – cold affected before warm leading to sensation of warmth by patients and finally temperature discrimination is lost.

c. Pin prick fibres

d. Fibres conveying pain greater than pin prick.

e. Touch fibres

f. Deep Pressure fibres

g. Somato motor fibres

h. Fibres conveying vibratory sense and proprioceptive impulses.

During recovery return of activity in the reverse order was assumed. Sympathetic fibres are the last to recover from blockade. (Collins et al).

FACTORS CONTROLLING THE LEVEL OF SPINAL ANESTHESIA

1. Effect of Gravity

- Specific gravity of local anaesthetic solution
- Baricity of the Solution
- Position of the patients

2. Effect of Volume

3. Concentrations of drug

4. Rate and force of injection

5. Site of injection

6. Pregnancy, large intra abdominal tumours, morbid obesity and other conditions leading to increased intra abdominal pressures.

7. Pressure of cerebro spinal fluid

8. Age.

FACTORS AFFECTING THE DURATION OF ANAESTHESIA

1. Dose and concentration of drug

2. Presence of vasoconstrictors which delays systemic absorption

CIRCULATORY EFFECTS OF SUBRACHNOID BLOCK

The preganglionic sympathetic fibres arise from the spinal cord between T1 and L2 and run in the corresponding anterior roots across the subarachnoid and epidural spaces. Most of the effects of spinal anaesthesia on cardiovascular system is due to the blockade of this preganglionic sympathetic fibres.

Hypotension following subarachnoid blockade is due to

(i) Sympathetic blockade leading to dilation of both resistance and capacitance vessels. Peripheral venous pooling which occurs causes reduction of venous return with subsequent fall in stroke volume and cardiac output.

(ii) Blocking of cardiac efferent sympathetic fibres form T1 to T4 resulting in loss of chronotropic and ionotropic drive to the heart, causing a fall in the cardiac output.

(iii) Paralysis of sympathetic nerve supply to the adrenal glands with consequent catecholamine depletion.

(iv) Blocking of muscular propulsive forces on the veins in the lower limbs, decreasing venous return.

Segmental blockade of the sympathetic nerves upto level T5 can be compensated in a normovolemic by vasoconstriction in the upper part of the body. This compensation occurs with little change in the cardiac output and with little more than 5% to 20% fall of the mean arterial pressure. Thus it is possible for a large part of arteriolar bed to be dilated under the influence of the sympathetic blockade while total peripheral vascular resistance changes little, due to compensatory vasoconstriction elsewhere. If the blockade extends beyond T4 and if more of the sympathetic outflow is

blocked including cardioacceleratory fibres, then it becomes more difficult to compensate for these haemodynamic changes and the blood pressure falls. If the pressure continues to fall below a certain critical level, it is probably due to an associated reduction of venous return and cardiac output.

The baro-receptors in the carotid sinus and aortic arch normally respond to a fall in blood pressure by producing compensatory tachycardia (Marey's Law) through vagal afferent and efferent pathways. Many patients under spinal anaesthesia exhibit bradycardia and hypotension and it appears that Bainbridge Reflex predominates. This reflex is mediated by the receptors in the great veins and right atrium which adjust the heart rate according to the venous filling pressures.

PHYSIOLOGY OF CEREBROSPINAL FLUID

CSF was discovered by Domenico Cotuqno and its circulation was described by F. Magendie. CSF an ultrafiltrate of plasma, is a clear, colourless fluid found in the ventricles of the brain.

Total volume of CSF ranges from 120-150ml of which 25-35ml is in the spinal subarchnoid space. CSF pressure ranges from 60-80 cm of water. It is formed by either secretion or ultrafiltration from choroid arterial plexuses of the lateral, III & IV ventricles.

Composition of CSF:

Protein	15-45 mg%
Glucose	50-80 mg%
Chloride	20-130 meq / lit
Sodium	40-150 meq / lit
Bicarbonate	25-30 meq / lit
Ph	7.4 – 7.6

Characteristics of spinal fluid:

Specific gravity – 1.003 – 1.009

Volume – 130 – 150 ml

Circulation of CSF:

Chroid plexus in the Lateral ventricles → through foramen of Manroe → 3rd Ventricle → Aqueduct of Sylvius → 4th Ventricle → through foramina of Luschka and Magendie → subarachnoid space.

PHYSIOLOGY OF SPINAL HYPOTENSION

Theories of causation of fall in blood pressure[1]

1. Reduced cardiac output due to reduction of venous return to heart and lack of propulsive force on veins.
2. Dilatation of post arteriolar capillaries and small venules due to paralysis of vaso constrictors.
3. Paralysis of sympathetic nerve supply to the heart (T^1 – T^4). Bradycardia may give rise to fall in cardiac output.
4. Paralysis of sympathetic nerve supply to the adrenal glands with consequent catecholamine depletion.
5. Absorption of drug into circulation.
6. Ischaemia and hypoxia of vital centers
7. Pre existing hypovolemia may give rise to severe fall in blood pressure if central neuraxial blockade is employed.
8. Compression of great vessels within the abdomen by the pregnant uterus or abdominal tumours or abdominal packs may cause severe hypotension in the presence of central neuraxial blockade.

Block not extending above T_4 is not always associated with fall in blood pressure in fit young adults.

Blood pressure fall is usually seen in the first 20 minutes after a block. Corrective measures may be considered if arterial pressure falls more than 20% of baseline value.

Treatment of spinal hypotension

1. Rapid infusion of I.V. Fludis
2. O2 inhalation
3. Foot end elevation
4. Injection of pressor drug – ephedrine or mephenteramine.
5. Injection of atropine if there is bradycardia.

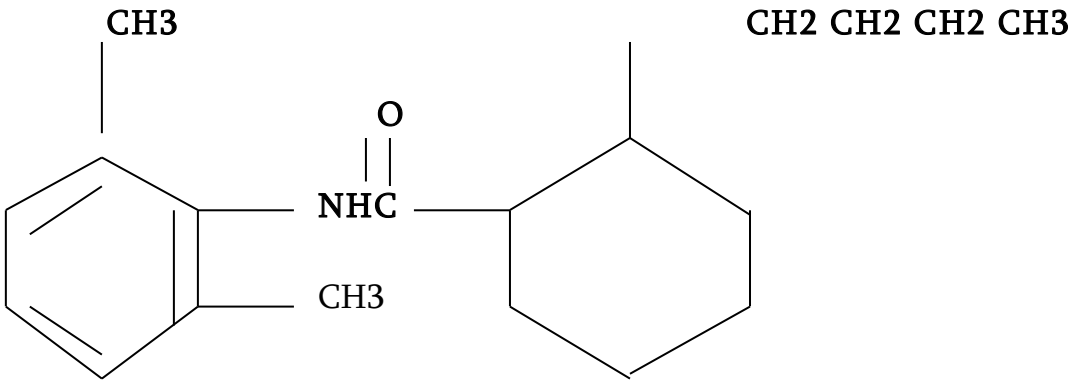
Preventive measures to reduce the incidence and severity of maternal hypotension associated with spinal anaesthesia.

1. Patient positioning to avoid aortocaval compression and promote cardiac preload.
2. Prehydration to expand blood volume, increase cardiac preload and thereby avoid the sudden decrease in cardiac preload.
3. Prophyactic or immediate use of appropriate vasopressors.

PHARMACOLOGY OF BUPIVACAINE [5]

Bupivacaine is an amide local anaesthetic introduced in 1963.

Structure



It is a hydrochloride salt of 1 butyl 2'6' pipecoloxylide and is presented as racemic mixture.It is a chiral drug as it possesses an asymmetric carbon atom.

It consist of lipophilic portion and hydrophilic portion separated by a connecting hydrocarbon chain. Hydrophilic portion is a tertiary amine and the lipophilic portion is an unsaturated aromatic ring such as paraamino benzoic acid.

The lipophilic portion is essential for anaesthetic activity .

Addition of butyl group to the piperidine nitrogen of mepivacaine results in bupivacaine which is 35 times more lipid soluble and has potency

and duration of action 3 to 4 times that of mepivacaine .

It is four times potent as lidocaine .It is slower in onset but has significantly longer duration of action.

Mechanism of action (Butterworth and strichasty 1990)

It prevents the transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion selective sodium channels in nerve membranes. This slows the rate of depolarization so that threshold potential is not reached and this action potential is not propagated.

Pharmacokinetics

It is rapidly absorbed from the site of injection. It has a long elimation half life (2.7hr) accompanied by low plasma clearance (0.58 l/min). These tend to increase the risk of systemic toxicity. It is 95% protein bound mainly α1 acid glycoprotein.

Most of the drug is metabolised in the liver by microsomal enzymes. Due to the slower metabolic rate this drug increases the risk of systemic toxicity and cumulative drug effects are more likely.

Poor water solubility of this drug makes the renal elimination of unchanged fraction to less than 5%.Only little amount crosses the placenta.

Pharmacodynamics

Onset of action is slow but it has longer duration of action. Increasing

the concentration of thisdrug will increase the degree of motor block.

Indications

Local anaesthesia
Any nerve block
Spinal Anaesthesia
Epidural Anaesthesia

Dosage

It is used in concentrations of 0.5% to 0.75 for spinal anaesthesia

Toxicity

Toxicity of this drug is due to the plasma concentration exceeding 1.5 to 2 μg / ml and is most likely due to the inadvertent intravenous injection.

Neurotoxicity is the most common side effect of this drug which will result in seizures. Mild side effects like restlessness , vertigo, slurred speech, muscle twitching will be followed by seizures. Later on CNS depression may follow which will produce hypoxia and apnea.

Cardiotoxicty is more in bupivacaine compared to equipotent dose of lignocaine. It may produce profound hypotension, dysrrhythmias and heart block. Dissociation of highly lipid souble bupivacaine from sodium channels receptors is slow accounting for persitent depression of myocardium.

PHARMACOLOGY OF EPHEDRINE [5,6]

History

It is an alkaloid obtained from Chinese herb Ma Huang. It was tasted by the Emperor shen Nung who placed it in the medium class. According to Pentsao Kang Ma Chinese dispensary written in 1596 by shih cheng le Ma Huang is of value as circulatory stimulant, diaphoretic, antipyretic, antitussive and it is an ingredient of many preparations.

Chen and schmidt introduced ephedrine into the western medicine in 1924 in the belief that actions of the drug were essentially sympathomimetic

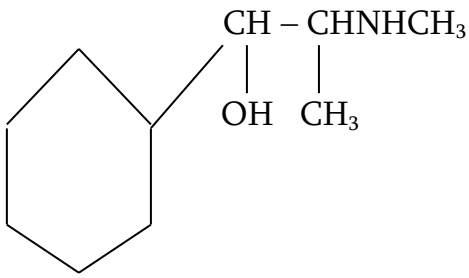
Chemical Name

(1R, 2S) 2 methylamino – 1, Phenylpropanolol

Chemical Formula

C_{10} H_{15} NO

Structure



Mechanism of action

Ephedrine has direct effect on stimulation of alpha and beta adrenergic receptors and indirect effect by liberating norepinephrine from the stores of neurons.

Pharmacologic properties

In cardiovascular system it produces vasoconstriction, increases cardiac contractility and increases heart rate. All these result in increased cardiac output and increased arterial pressure.

Stimulation of B_2 adrenergic receptors at bronchial smooth muscle produces bronchodilation and at urinary system it produces sphincter contraction and relaxation of vesical wall which causes urinary retention.

It has very little effect on uterine activity.

In CNS it produces stimulation.

In GI system it reduces intestinal tone and motility.

It dilates the pupil but does not affect light reflexes.

Pharmaco kinetics

Bioavailability after oral route of absorption is 85% producing peak effect in 1 to 2 hrs. With topical administration absorption is 64%.

Onset of action

It has immediate effect in intravenous form, by intramuscular route onset is 10 to 20 minutes and in oral & subcutaneous route it has gradual onset.(20 to 30 minutes)

Duration of action

Vasopressor and cardiac effects are observed upto 60 min if administered by intramuscular route. By oral route its effect may last upto 5 hrs and by intranasal route decongestant effect last for 3 to 6 hrs.

Metabolism

It is metabolized by oxidative deamination, desmethylation, aromatic hydroxylation and conjugation. It is resistant to the action of MAO(MonoAmine Oxidases) and COMT.(Catechol-o-Methyl Transferases)

Excretion

By renal route depending on urinary PH. Elimination is enhanced and halflife is shorter in acidic urine.

Preparations and routes of administration

15 mg Tablets

30mg / ml Ampoules

It can be administered by oral, subcutaneous, intramuscular or intravenous routes.

Therapeutic uses

1. It is used to prevent or treat hypotension induced by spinal or epidural anaesthesia.
2. As a bronchodilator
3. As nasal decongestant
4. to treat post operative nausea & vomiting
5. To treat urinary incontinence
6. Treatment of nocturnal enuresis
7. Treatment of obesity
8. As mydriatic

Adverse effects

CVS – Palpitation, Tachycardia, Hypertension

CNS – Nervousness, Fear, Anxiety, Hallucinations, Psychosis and Depression with chronic use.

Genitourinary system: Urinary retention

Skin - Hypersensitivity, Rashes

In Fetus- Hyperactivity, Irritabilty & Fetal Tachycardia.

Miscellaneous

Dry mouth

Tremor

Tachyphylaxis with repeated use

Precautions to be taken in cases of

Prostatic Hypertrophy

Arterial Hypertension

Coronary artery disease

Diabetes mellitus

Hyperthyroidism

Renal impairment / closed angle glaucoma.

Drug interaction

Administration of ephedrine may cause hypertensive crisis in patients receiving MAOI. It may cause arrythmias in patients receiving ergot alkaloids or oxytocin .

REVIEW OF LITERATURE

Hypotension is the most important complication following spinal anaesthesia various methods have been studied to prevent hypotension.

Lot of literature supporting parenteral administration of prophylactic ephedrine are available but, only few literatures supporting prophylactic oral ephedrine are available.

Though many pressor agents are available to prevent & treat hypotension, ephedrine remains the standard drug for spinal induced hypotension.

Kafle, Malla and Lekhak [7] in 1994 studied the efficacy of oral ephedrine for prevention of spinal induced hypotension in two hundred women of ASA class I and II undergoing lower abdominal surgeries. The patients were divided into two groups randomly (n = 100 each).

All patients were given routine oral premedication consisting of diazepam 10mg and ranitidne 150mg at bed time and at 90 min before surgery. In addition Group I patients received ephedrine 30mg orally 30min before subarachnoid block was administered. Group II received only routine premedication. After starting IV line and preloading with 10 ml/kg crystalloid , patients were given 0.5% heavy bupivacaine 3.2 to 3.6ml

depending on body

weight intrathecally. Patients with decreases in blood pressure of more than 20% of baseline systolic value were given ephedrine IV in increments in addition to crystalloids. Despite a similar level of block (T_3 – T_4) and IV fluids, the total dose of ephedrine supplement in Group I was 4.3 +/- 4.8 mg compared with 11.6 + % 9.4 mg in Group II (P<0.01) Also 55 patients in Group I, required intraoperative ionotrope supplement compared with 83 in Group II (P < .0.01).

They concluded that oral ephedrine premedication is a simple and effective way of reducing the incidence of hypotension in patients undergoing lower abdominal surgeries under SAB.

Fusun eroglu [8] et al studied prophylactic effects of systemic oral ephedrine in spinal Anaesthesia induced hypotension during TURP, at dept of Anesthesiology. Suleiman Demirel university Ispaita, Tulkey.

They studied sixty ASA Grade II and II patients scheduled for spinal Anesthesia.

They were randomly divided into two groups. Patients in Group I (n = 30) received oral ephedrine 50mg in addition to premedication whilst those in Group II (n = 30) received only premedicaiton 30min before spinal

anaesthesia. Hypotension was defined as SAP < 20% of baseline value and was

treated with 3mg ephedrine and bradycardia was corrected with atropine 0.5mg given as an iv bolus.

They found that SAP values were significantly lower in group II during spinal. Post spinal & intraoperative periods, (P<0.0001). 15 patients received ephedrine in Group II and seven in Group I .Supplemental ephedrine was used at doses of 3.42 ± 0.97 mg in Group I and 8.86 ± 1.20mg in group II. The incidence of hypotension was halved in group I compared to Group II (23.33 % Vs 50%, p < 0.003) Six patients received atropine in Group II because of severe bradycardia. Mean HR values were lower in Group II than Group I during study period.

They concluded that prophylactic oral ephedrine at 50mg dose is effective for measuring spinal induced hypotension during TURP.

Subbiah et al studied at Madurai Medical College 50 patients of ASA I undergoing elective LSCS to evaluate the efficacy of prophylactic oral ephedrine 30mg to prevent spinal hypotension. Study was conducted in double blind randomized controlled trial and they found out that prophylactic administration of oral ephedrine is associated with lower

incidence of hypotension after SAB in LSCS when compared to control group and has no side effects.

PF Kotur et al have done a randomized clinical trial of comparison of prophylactic oral ephedrine and control in reducing the incidence of hypotension after SAB at JN Medical college. Belgaum, Karnataka. They studied 100 patients of both sexes between the age group of 20 – 60 yrs belonging to ASA I & II scheduled for elective lower abdominal surgeries under SAB and found that prophylactic administration of oral Ephedrine was associated with lower incidence of hypotension after SAB with (22% Vs 76%) when compared to control group.

T. Kushimo et al at Nigeria studied sixty patients for elective caesarian section randomly allocating into two groups. One group was infused with 1L of 0.9% saline before spinal block and group 2 was infused with ephedrine 30mg in 1 L of 0.9% saline after spinal block and concluded that prophylactic ephedrine given by standard infusion set was more effective than any standard infusion set was more effective than crystalloid prehydrasion in prevention of Hypotension during spinal for elective caesarian section.

Loughery JP. Walsh f, Gardiner J [9] at Ireland did a randomized control study in 68 patients undergoing SAB the efficacy of prophylactic

intravenous ephedrine in prevention of spinal induced hypotension with 2 ml of 0.9%

saline in one group , 6mg ephedrine IV in 2nd Group and 12mg ephedrine in 3rd group and concluded that prophylactic bolus of ephedrine 12mg IV given at the time of intrathecal block leads to lower incidence of hypotension following spinal Anesthesia for elective LSCS patients.

Ayorinde BT [10] et al UK studied 108 patients undergoing elective LSCS under SAB, assigned to four groups in a randomized double blind placebo controlled study, Group I received preemptive phenyl ephrine 4mg im , group 2 received phenylephrin 2mg im and group 3 received ephedrine 45mg im while control group received im injection of saline, all given immediately after spinal anesthesia. They found out that incidence of hypotension was 33% in phenylephrine 4mg group, compared with 70% in control group & phenylephrine 2mg group and 48% in the ephedrine group .

Simon L [11] et al studied 108 women undergoing elective LSCS under spinal anesthesia by giving 10, 15, 20mg ephedrine IV bolus 2 minutes after intrathecal injection as prophylaxis and concluded that single bolus of IV ephedrine with doses of either 15 or 20mg decreased significantly the

incidence of maternal hypotension as compared to a single 10mg bolus of ephedrine.

Gajaraj NM [12] et al compared ephedrine infusion with crystalloid administration for prevention of hypotension during spinal anesthesia in 54 ASA I patients undergoing postpartum tubal ligation under spinal anesthesia. One group received 15 ml/kg of crystalloid and other group received ephedrine infusion and concluded that prophylactic ephedrine influsion is effective for minimising and managing hypotension associated with spinal anaesthesia and also found that reactive hypertension or tachycardia did not occur in the ephedrine group.

Rout CC [13] et al reevaluated the role of crystalloid preload in the prevention of hypotension associated with the spinal anesthesia for elective caesarian section, in 140 patients of two groups, one with 20 ml/kg of crystalloid administration and another group with out crystalloid administration and found that crystalloid administration was not effective in preventing hypotension.

Hemmingsen C [14] et al studied 48 patients undergoing LSCS under spinal anaesthesia to know the efficacy of prophylactic im ephedrine in two different doses of 12.5mg and 37.5mg and found that prophylactic ephedrine is desirable in spinal anaesthesia .

Sternlo JE [15] et al investigated the efficaly of im ephedrine in 98 elderly patients undergoing hip arthroplasty under spinal anaesthesia. 50 patients were given 0.6 mg / kg of ephedrine deep in the paravertable muscles immediately after spinal and 48 patients received equal volume of saline and concluded that prophylactic im ephedrine is a simple and effective means of reducing the incidence of hypotensive episodes.

Jackson. R [16] et al compared the protective effect of 1000ml preload with 200ml preload of crystalloid solution administrated during 10 min before spinal anaesthesia in 60 women undergoing LSCS and found that crystalloid preloading is not effective.

Webb AA [17] et al assessed the efficacy of prophylactic im ephedrine to prevent hypotension in spinal Anaesthesia for caesarian section. 40 patients divided into two groups of 20 each. One group received 37.5mg im ephedrine and other group received placebo and they found that incidence of hypotension is less in ephedrine group.

Di Roio C [18] et al studied 20 patients aged 60 yrs or more of ASA class II or III scheduled for surgical correction of Fractured neck of femur under SAB. One group (n=10) received ephedrine 30mg intramusculary immediately after SAB. The other group received 1ml of saline intramuscularly. They found that prophylactic intramuscular ephedrine is

effective to prevent hypotension associated with SAB.

Kee WD [19] et al studied 80 women undergoing LSCS divided into 4 groups of 20 each receiving saline, ephedrine 10mg, 20mg, or 30mg IV, 1 minute after intrathecal injection and concluded that ephedrine 30mg dose was effective in reducing incidence of hypotension.

Vercauteren MP [20] et al studied 50 patients undergoing spinal anaesthesia and compared the efficacy of prophylactic ephedrine 5mg im Vs saline IV to prevent spinal hypotension and found that prophylactic ephedrine decreases the occurrence and reduces the severity of hypotension.

Butterworth et al found that a mixed adrenergic agonist such as ephedrine more ideally corrected the non cardiac circulatory sequelae of total spinal anaesthesia in dogs than did either a pure alpha (Phenylephrine) or a pure beta adrenergic agonist (isoproterenol)

Goertz et al investigated the effect of ephedrine on left ventricular function in patients without cardiovascular disease under high thoracic epidural analgesia combined with General Anaesthesia. Ephedrine improved left ventricular contractility without causing relevant changes of left ventricular after load.

MATERIALS & METHODS

After getting ethical committee approval and informed consent a randomised clinical study was conducted in 100 ASA class I men undergoing elective lower abdominal and scrotal surgeries under spinal anaesthesia to evaluate the efficacy of prophylactic oral ephedrine in prevention of spinal induced hypotension.

This study was carried out in Govt. Stanley medical College, Chennai during the period of Oct 2005 to Oct 2006.

Inclusion criteria were

1. ASA Class I patients
2. Age between 25-55 Yrs
3. Patients coming for lower abdominal and scrotal surgeries.

Exclusion criteria were

1. obesity
2. Height less than 155cm
3. Diabetes
4. hypertension
5. Ischaemic heart disease
6. Chronic renal failure
7. Anaemia

8. Bleeding disorders

9. Epilepsy

Preoperative preparation

Thorough preoperative assessment with detailed medical history, physical examination and investigations were carried out. Each patient was explained about the procedure and type of anaesthesia and informed consent was obtained.

All patients were advised to fast 6 hrs for solids and 4 hrs for liquids before surgery and no intravenous fluids were administered until the patients arrived in the premedication room. All the patients were premedicated with 10mg of Tab.diazepam and 150mg of Tab. Ranitidine at bedtime on the previous night of surgery. No premedication was given in the morning of surgery.

Investigations

Hb%,PCV

Total Count

Differential count

Blood sugar

Blood Urea

Serum creatinine

Bleeding time

Clotting time

Platelet count

Urine analysis for Albumin sugar and deposits

ECG

Chest X – Ray

And relevant investigations if needed .

These 100 patients were randomly allocated into two groups of 50 each. Patients in Group E (ephedrine group) received 30mg of Tab. Ephedrine with sips of water 30min prior to spinal anaesthesia and patients in group C (control group) received no tablets.

Average of three readings of blood pressure at 5 minutes intervals prior to administration of Tab ephedrine & iv fluids was taken as baseline blood pressure. Similarly baseline heart rate and SPO_2 were measured.

Patients were shifted to operation theatre 20 minutes prior to administration of spinal anaesthesia and were connected to multipara monitor and NIBP, ECG, SPO_2 were monitored continuously. An IV Access using 18 g iv cannula established over the left forearm under aseptic precautions. Patients in both groups were preloaded with 10 ml/kg of Ringer lactate over a period of 15 minutes.

Anaesthesia

At the end of 15min(ie after preloading) patient was placed in right lateral postion. Under aseptic precautions and draping L3 L4 inter vertebral space was identified and sub arachnoid block was performed with 23G quinke Babcock spinal needle after ensuring free flow of cerebro spinal fluid. Depending upon the weight and height of the patient 3.2 to 3.5 ml of 0.5% hyperbaric Bupivacaine was injected slowly over a period of 20 seconds. Immediately after injection of the drug ,patient was turned to supine position.

Level of sensory block was assessed using pinprick sensation. Once the level reached T6 –T8, the level of block was optimized by giving 10^0 head tilt position or keeping pillow under the chest and head till the fixation of drug i.e 20 – 30 minutes. Crystalloid at the rate of 10ml / kg / hr was used for maintenance during the intra operative period.

All patients were sedated with 1.5mg of midazolam 5min prior to skin incision

Monitoring

All the patients were monitored throughout the procedure. Systolic Blood Pressure, Diastolic blood pressure and mean arterial blood pressure were monitored by noninvasive automated oscillatory method and Heart

rate was measured by ECG, before spinal and immediately after spinal anaesthesia.

Similarly during intraoperative period readings were taken at the interval of 3minutes upto first 15 minutes, then every 5 minutes till 30th minute, every 10 minutes till 60th minute and every 15minutes till 120 minutes. All these readings were recorded in the master chart.

Other parameters such as SPO2 ,urine output, were also monitored. Blood loss was assessed.

Hypotension was defined as decrease in systolic BP of more than 20% of Baseline value. Hypotension was treated with IV fluids and inj.Ephedrine IV boluses of 6mg increments. Bradycardia was defined as heart rate less than 60/min and treated with inj. Atropine 0.3 mg increments.

The patients were observed in the recovery room & Blood pressure and other vital parameters were monitored every 30 minutes thereafter till the complete regression of the sensory & motor blockade

The following parameters were observed post operatively in the post op ward. Heart rate,Resp Rate,Oxygen Saturation,Blood Pressure

1. Urine Output
2. Side effects like dry mouth, headache, palpitations, urinary retention, anxiety ,restlessness, tremor, nausea and vomiting.

OBSERVATIONS AND RESULTS

Table 1

Physical Parameters

S.No	Physical Parameter	Control gp		Ephedrine group		Pvalue	Significance
		Mean	SD	Mean	SD		
1	Age (Yrs)	37.96	7.93	38.84	8.53	0.498	Not. signifi
2	Height (cm)	166.7	3.18	166.3	2.93	0.323	Not. signifi
3	Weight (Kg)	58.52	4.19	58.78	4.11	0.632	Not. signifi

Table 2

Mean Systolic BP. Baseline

S.No	Group	No of Cases	Mean	SD	Pvalue	Significance
1	Control	50	119.06	7.18	0.146	Not Signt
2	Ephedrine	50	119.38	9.3		

Table 3

Mean Diastolic BP. Baseline

S.No	Group	No of Cases	Mean	SD	Pvalue	Significance
1	Control	50	75.56	5.50	0.542	Not Signt
2	Ephedrine	50	76.72	4.82		

Table 4

Mean of Mean Arterial Pressure Baseline

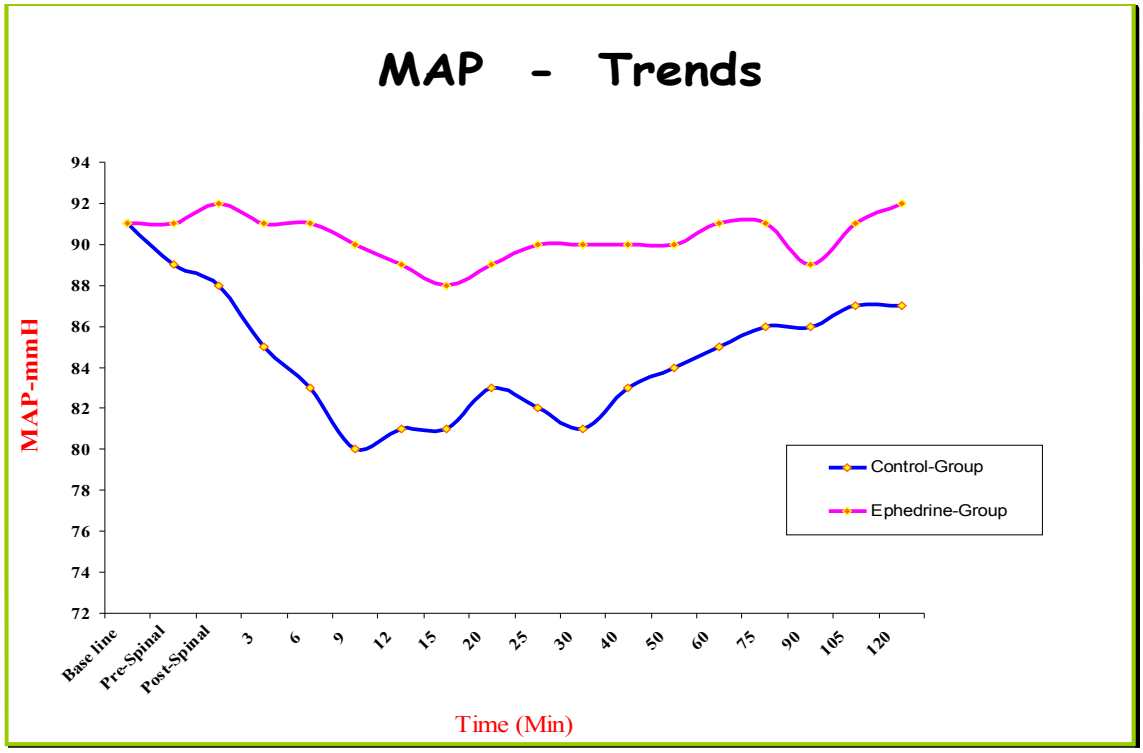
S.No	Group	No of Cases	Mean	SD	Pvalue	Significance
1	Control	50	90.76	6.33	0.653	Not Signt
2	Ephedrine	50	90.74	5.46		

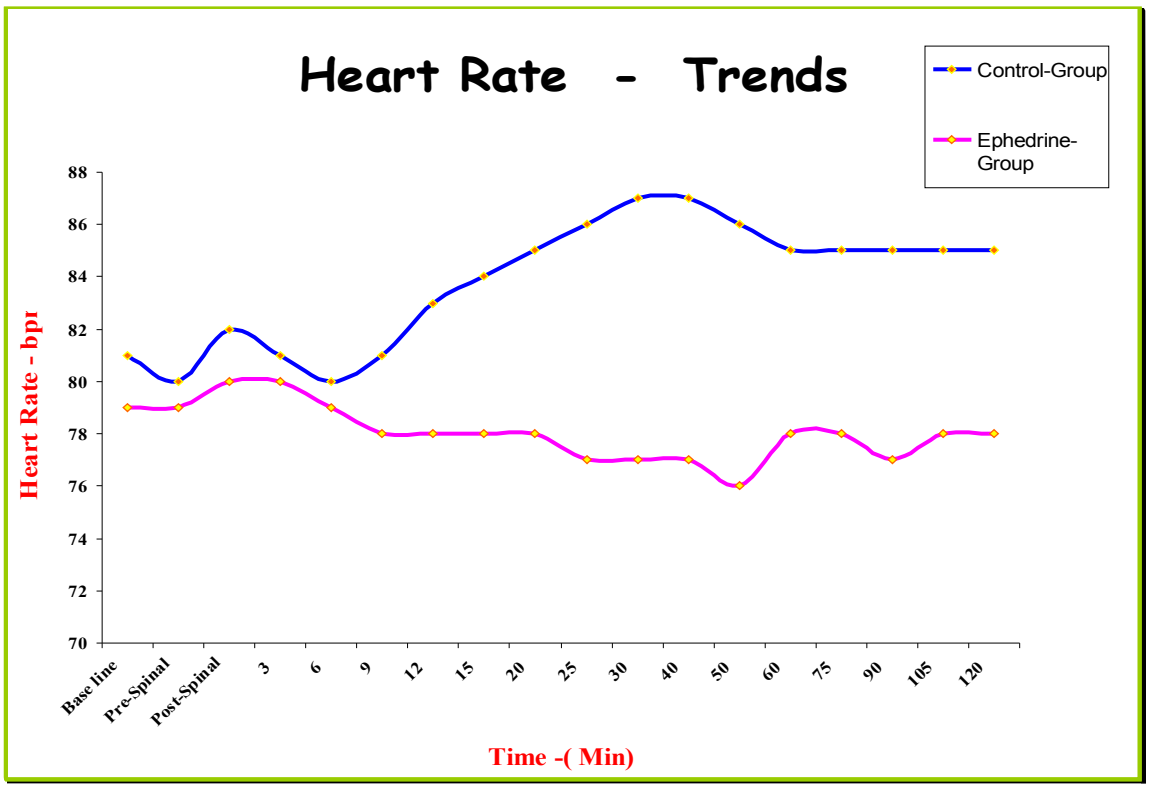
Table 5

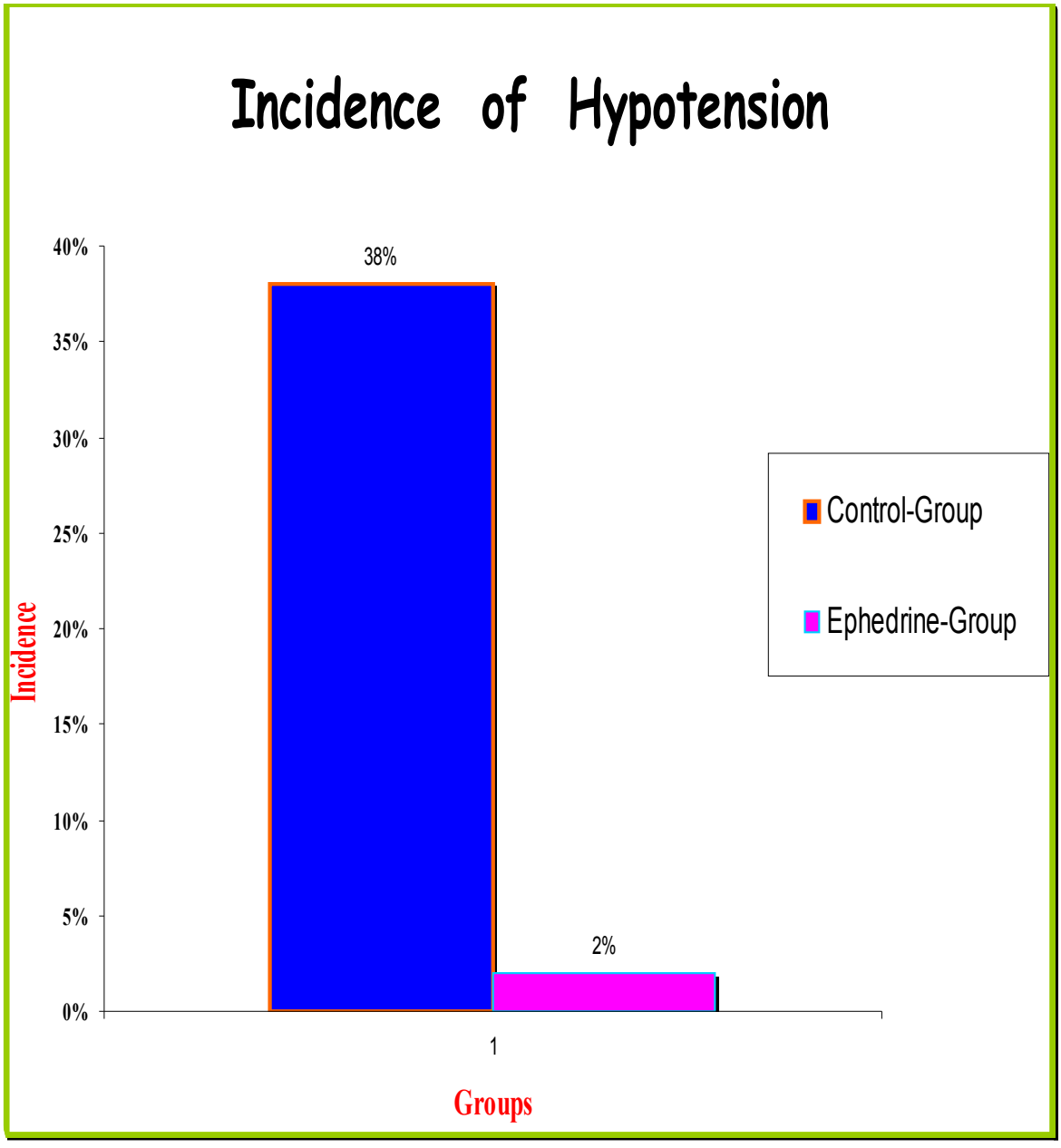
Mean Heart rate Baseline

S.No	Group	No of Cases	Mean	SD	Pvalue	Significance
1	Control	50	80.98	7.30	0.210	Not Signt
2	Ephedrine	50	78.94	7.79		

Table 6




Heart Rate - Trends
Control-Group
Ephedrine-Group
Heart Rate - bpr
88
86
84
82
80
78
76
74
72
70
Base line
Pre-Spinal
Post-Spinal
3
6
9
12
15
20
25
30
40
50
60
75
90
105
120
Time -(Min)


Incidence of Hypotension
40%
35%
30%
25%
20%
15%
10%
5%
0%
Incidence
38%
2%
1
Groups
Control-Group
Ephedrine-Group

DISCUSSION

Hypotension is one of the most common complications in patients undergoing spinal anaesthesia which cam compromise the perfusion of vital organs like Heart, brain & kidneys and can cause irreversible insult to these organs. Various methods have been employed to prevent this detrimental complication out of which prophylactic use of Ephedrine was found to be most effective. This correlates with the study done by **Gajraj NM** [12] et al which concludes prophylactic ephedrine infusion was more effective than crystalloid preloading in prevention of spinal hypotension.

Various studies as discussed in review of literature have used prophylactic ephedrine in various routes such as IM, IV bolus, IV infusion and Oral route as prophylaxis for spinal hypotension.

Our study was done to show the efficacy of oral ephedrine Tablets in preventing spinal hypotension. If found to be effective it could be one of the simplest methods of preventing this lethal complication of spinal anaesthesia.

Ephedrine is one of the most commonly used drugs in the prevention & treatment of spinal hypotension. It stimulates both ά and β receptors and releases nor epinephrine from neuronal strores. It is also orally effective as

its oral bioavailability is 85%. Its onset of action is 30 – 45 minute given orally and duration of action is 3 to 5 hrs. This substantiates the selection of our study .

100 patients of ASA class I men undergoing various lower Abdominal & scrotal surgeries were chosen between the age group of 25-55 yrs and were randomly allocated into two groups of 50 each. Group E (Ephedrine gp) patients received 30mg of oral ephedrine 30min prior to spinal anaesthesia with sips of water. Group C (Control gp) patients received no tablets. Preloading with 10ml/kg of Ringer lactate was done in both the groups over the period of 15 min after which spinal anaesthesia was given.

The dosage of ephedrine and the onset of action were supported by the textbook description and previous studies done by **kafle** [7] et al, **fusun eroglu** [8] et al **subbiah** et al and **PF kotur** et al.They all concluded that oral ephedrine prophylaxis significantly reduces the incidence of spinal induced hypotension. If 3.2 to 3.5 ml of 0.5% (H) Bupivacaine was used for spinal anaesthesia. It was given in L3 L4 space with patient in Right lateral position. Immediately after spinal the patient was turned to supine position with 10^0 head up tilt till the fixation of drug and the level of block was optimized between T6 – T8.

Monitoring of the patients was done from administration of

ephedrine to the end of surgery and there after in the recovery room and postoperative ward till complete regression of spinal anaesthesia.

Hemodynamic parameters such as systolic, diastolic, mean arterial pressure and Heart rate were measured at baseline, prespinal, post spinal, 3minutes interval upto 15minutes, 5minutes interval upto 30^{th} minute, 10minutes interval till the 60^{th} minute 15 minutes interval upto 120^{th} minutes and recorded in the master chart.

Statistical analysis was done using students T test and chi square test to compare the variables in both the groups.

Physical parameters such as age, height and weight in both groups were compared and it was found that 'P' value was not significant which states that patients in both the groups were similar in terms of physical parameters.

Baseline systolic, diastolic, mean arterial pressures in both the groups were analysed and found that P values were not significant which states that patients in both the groups were similar in terms of baseline hemodynanmic parameters.

Hypotension was defined as fall in systolic BP, more than 20% of baseline value, and was treated with inj. Ehedrine 6mg iv in increments till it reached within 20% of baseline value. Heart rate less than 60/min s

treated with inj atropine 0.3mg increments.

Kafle [7] et al have taken fall in SBP more than 20% of baseline value as significant hypotension in their study.

Fusun eroglu [8] et al also had taken fall in SBP more than 20% of baseline value or less than 100mm Hg as significant hypotension in their study.

Rout CC [13] et al took < 80% of Baseline SBP or < 100 mmHg from baseline as hypotension in their study of evaluation of crystalloid preload in the prevention of spinal hypotension.

In our study fall in Systolic BP more than 20% of baseline value was taken as hypotension. We found that 19 patients in the control group & one patient in ephedrine gp developed hypotension (ie SBP falling < 80% of baseline value). Statistical analysis was carried out and found that the incidence of hypotension is 38% in the control group and 2% in the Ephedrine group (P value = 00001 ie. < 0.05) P value was significant showing that incidence of hypotension due to spinal anaesthesia is negligible in ephedrine group.

Kafle [7] et al found that incidence of hypotension in ephedrine group was less (55%) Compared to control group (83%) (P value 0.01) which correlates our study.

Fusun eroglu [8] et al in their study found that the incidence of hypotension is less in ephedrine group (23.33%) than control group(50 %) p value was 0.003 which is significant and this substantiates our study.

Subbiah et al found out in their study that incidence of hypotension is less in the ephedrine group compared to control group.

Kotur PF et al also found that incidence of hypotension is nil in ephedrine group (0%) compared to control group (22%).

All those studies & various other studies mentioned in review of literature using intramuscular, intravenous bolus or infusion ephedrine have proved that incidence of hypotension is less in ephedrine group which support our study result.

In our study we found that none of the patients in the ephedrine group showed reactive hypertension or tachycardia. They didn't have any side effects such as palpitation ,dry mouth, restlessness, tremor, nausea and vomiting during intraoperative period or the post operative period.

Kafle [7] et al and various other studies have shown that no adverse effects were observed in the ephedrine group in 30mg doses which correlates with our study.

SUMMARY

In our study 100 ASA class I men scheduled for elective lower abdominal & scrotal surgeries under spinal anaesthesia were randomly divided into 2 groups. Group I patients (n = 50) received tab. Ephedrine 30 mg and Group II (control) patients did not receive tab Ephedrine

We found out that Group I receiving Tab. Ephedrine 30mg had lower incidence of hypotension (2%) compared to Group II (Control) (38%) and did not report any side effects.

CONCLUSION

From our study we conclude that oral ephedrine prophylaxis is a simple, easy, economical . effective and reliable method in reducing the incidence of hypotension following subarachnoid block in patients undergoing elective lower abdominal and scrotal surgeries and does not have any adverse effects.

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PROFORMA

One year randomized study of comparison of prophylactic Oral ephedrine and control (without ephedrine) in reducing the incidence of hypotension after subarachnoid block in patients undergoing elective lower abdominal and scrotal surgeries .

Name IP No ASA Grade

Age; ward

Preoperative diagnosis

Surgery performed

Surgeon

Anaesthesiologist

Physical examination

General examination

Build pallor cyanosis

Weight icterus clubbing

Pedal ederna lymphadenopathy

Vital parameters

Pulse rate

Blood pressure

Respiratory rate

Systems examination

(i) cardiovascular system

(ii) Respiratory system

(iii) Central nervous system

(iv) Gastro intestinal system

(v) Renal system

Investigations

Complete blood count

Urine routine examination

Random Blood sugar

Blood urea

Serum creatinine

Premedication

Tab. Ranitidine 150 mg Tab. Diazepam 10 mg	Night befoe surgery for Both groups

Group E

Tab. Ephedrine 30mg. with sips of water 30 min before subarachniod block.

Group P.

None

Preoperative Pulse rate

Blood pressure

Anaesthesia

Procedure	:	Rubarachnoid block
Posture	:	Right lateral
Site	:	L3 L4 subarachnoid space
Drug	:	Inj Bupivacame
Concentration	:	0.5% Heavy
Dose	:	3.2 to 3.5 ml

Level of Anaesthesia

Intra operative period

Monitoring

S.no Parameter Baseline Prespinal Post spinal 3,6,9,12,15,20

1. Pulse rate
2. Systolic Blood pressure
3. Diastolic Blood pressure
4. SPO_2

25 30 40 50 60 75 90 120 min

Pulse rate

1. Systor Blood pressure
2. Dlastolic Blood pressure
3. SPO2

IV fluids Blood Drugs

Blood loss

Urine